

- SUB  
E1  
CONT.
- D1  
(cont.)
- to primers in a manner to allow primer extension in the presence of nucleotides and a nucleic acid polymerase;
- c) providing each location with a nucleic acid polymerase and a given labelled nucleotide under conditions that allow extension of the primers if a complementary base or if a plurality of such bases is present at the appropriate position in the single stranded nucleic acid molecules;
- d) detecting whether or not said labelled nucleotide has been used for primer extension at each location by determining whether or not the label present on said nucleotide has been incorporated into extended primers and if said labelled nucleotide has been used in primer extension this step involves detecting how many of said nucleotides have been used per extended primer;
- e) repeating steps c) and d) one or more times without removing incorporated labels so that extended primers each comprising a plurality of labels are provided;

whereby the sequence of the nucleic acid molecules at the first and second locations is obtained by reference to the number and type of nucleotides used in primer extension at these location.

SUB  
E4

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17. (Thrice Amended) A method for sequencing nucleic acid molecules, comprising the steps of:

- a) providing at a first location a plurality of single stranded nucleic acid molecules that have the same sequences as one another and that are hybridized to primers in a manner to allow primer extension in the presence of nucleotides and a nucleic acid polymerase;
- b) providing at a second location, which is different from the first location, a plurality of single stranded nucleic acid molecules that have the same sequences as one another, but that have different sequences from the sequences of the single stranded nucleic acid molecules at the first location, and that are also

- hybridized to primers in a manner to allow primer extension in the presence of nucleotides and a nucleic acid polymerase;
- c) providing each location with a nucleic acid polymerase and a given nucleotide in labelled and unlabelled form under conditions that allow extension of the primers if a complementary base or if a plurality of such bases is present at the appropriate position in the single stranded nucleic acid molecules;
- d) detecting whether or not said labelled nucleotide has been used for primer extension at each location by determining whether or not the label present on said nucleotide has been incorporated into extended primers, and if said labelled nucleotide has been used in primer extension, this step involves detecting how many of said nucleotides have been used per extended primer;
- e) repeating steps c) and d) one or more times without removing incorporated labels so that extended primers each comprising a plurality of labels are provided;

whereby the sequence of the nucleic acid molecules at the first and second locations is obtained by reference to the number and type of nucleotides used in primer extension at these location.

21. **(Thrice Amended)** A method of sequencing a target nucleic acid comprising:
- (a) hybridizing the target nucleic acid to a primer whereby the target nucleic acid can serve as a template for extension of the 3' end of the primer;
- (b) incubating the hybridized target nucleic acid/primer with a polymerase and a type of nucleotide bearing a label under conditions supporting template-directed extension of the primer if the nucleotide type can be incorporated as the complement of a corresponding nucleotide of the target;
- (c) measuring first label incorporated into the primer to determine whether, and if so, by how many base increments, the primer has been extended by incorporation of the nucleotide type;

- sub  
E10  
cont
- 3  
D  
(cont)
- (d) incubating the hybridized primer/target nucleic acid with a different type of nucleotide bearing a label under conditions supporting template-directed extension of the primer if the different nucleotide type can be incorporated so as to be complementary to a corresponding nucleotide in the target;
  - (e) measuring incremental label incorporated into the primer due to the previous incubating step to determine whether, and if so, by how many base increments, the primer has been extended by incorporation of the different nucleotide type; and
  - (f) repeating steps (b) - (e) without removing incorporated labels so that extended primer comprising a plurality of labels are provided, until a desired portion of the target sequence can be determined from the incremental base additions to the primer.